

Case Report

Gall bladder cancer – Radical surgery, the key role to improve outcome

P Bhuta, M G Brown, J M Alderdice

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Gall bladder cancer is one of five most common malignancies of the gastro-intestinal tract. Most of the cancers are detected during histological examination after cholecystectomy. Females are more commonly affected than males with a ratio of 4:1. A direct association exists between the presence of cholelithiasis and the development of gall bladder carcinoma. In patients with gall bladder carcinoma the incidence of cholelithiasis ranges from 54-97 percent. Adenocarcinoma is the most common histological type but others can occur. We present four cases seen by a single surgeon in general surgical practice, during a four-year period. These cases demonstrate the varying histological types and the management of gall bladder carcinoma.

CASE 1 An 82 year old female admitted with bleeding per rectum. She had recently been seen in the outpatients and investigated for bleeding PR. A barium enema carried out at this time was normal. The patient was later admitted as an emergency with haematemesis along with fresh bleeding per rectum. The patient was taken for an urgent upper gastrointestinal endoscopy which showed bright red blood in the duodenum. After resuscitation, the patient was taken to theatre for an exploratory laparotomy. The intraoperative findings were those of a duodenocolic fistula associated with an inflamed gangrenous gall bladder. The fistula was closed and a cholecystectomy performed. Histopathology showed one of the rarer types of gall bladder carcinoma, namely a well differentiated, keratinising squamous-cell carcinoma, forming squamous pearls (figure 1). The carcinoma had invaded through the wall to the serosal surface. Post operatively she made a good-recovery. A referral was made to the oncology team for post-operative radiotherapy. The patient was admitted

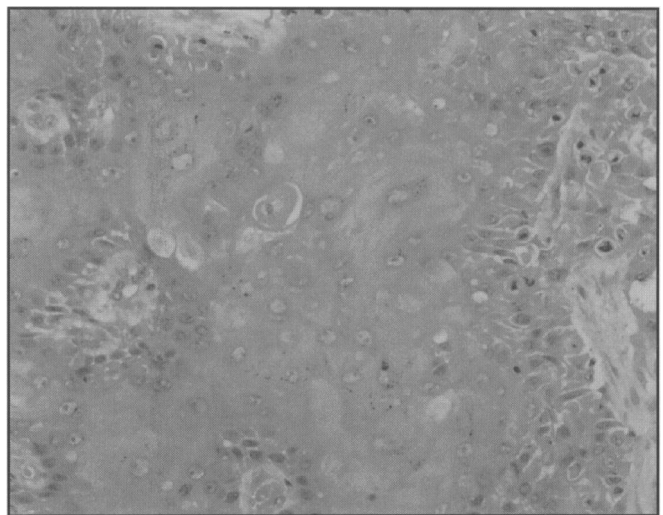


Fig 1.

again 3 months later with vomiting, upper abdominal pain and jaundice. Her condition deteriorated rapidly and she died four days later due to widespread metastatic disease.

CASE 2 A 69 year old female with a history of gall stones was admitted with recurrent episodes of pain in the right hypochondrium. An ultrasound showed a soft-tissue echo in the region of the gall bladder. CT scan subsequently showed a solid lesion also in the region of the gall bladder not typical of a gall stone. It was decided to proceed with a laparoscopic cholecystectomy. During the procedure it was impossible to hold the gall bladder as it was hard and tense. The procedure was converted to an open procedure. The gall

Causeway Hospital, Coleraine, Co. Londonderry.

P Bhuta, FRCS, Surgical Registrar

M G Brown, MD, FRCS, Consultant Surgeon

Dr J M Alderdice, FRCPath, Consultant Pathologist

Correspondence to Mr Bhuta

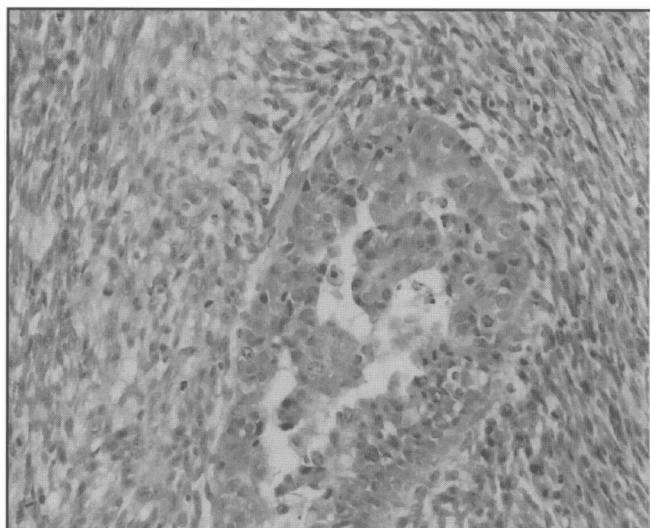


Fig 2.

bladder was solid and contained no bile, therefore along with cholecystectomy an adjacent cuff of the liver was removed. Histopathology showed a very rare, locally advanced primary malignancy of gall bladder with spread to the liver bed. The resection margins were clear. There was a biphasic pattern of malignant glands set in a malignant stroma in keeping with a carcinosarcoma (figure 2). This type of malignancy is probably primarily adenocarcinomatous with foci of sarcomatous change in poorly differentiated areas. Immediate post operative CT scan of the liver showed metastatic disease. The patient was treated with postoperative radiotherapy and palliative chemotherapy. Her last follow-up showed no change in the metastases in the liver on MRI.

CASE 3 A 75 year old female was referred with a history suggestive of obstructive jaundice secondary to gall stones. An abdominal scan

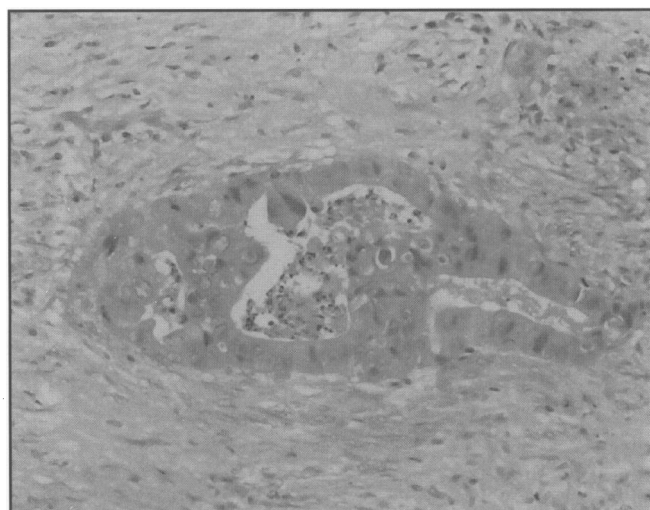


Fig 3.

showed multiple gall stones with a normal calibre common bile duct. The patient settled down on conservative management. A subsequent ERCP was normal. She underwent an elective laparoscopic cholecystectomy for gall stones six months later. Histopathology of the gall bladder showed a dysplastic lining mucosa from which a regular type, moderately well differentiated invasive adenocarcinoma was taking origin, and infiltrating to the circumferential limit (figure 3). The patient was offered further surgery but this was declined. The patient is being followed up and CT carried out one year after surgery does not show any evidence of metastatic disease.

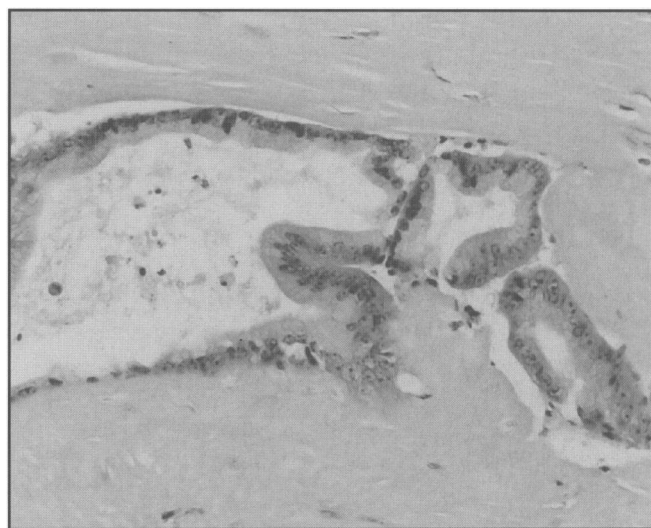


Fig 4.

CASE 4 A 70 year old female was admitted with a history of painless jaundice. An ultrasound scan showed a stone in the lower common bile duct. Considering the severity of jaundice and the size of the stone it was decided to proceed with open surgery. Cholecystectomy and common bile duct exploration were carried out and the stone was removed with the help of a choledochoscope. Histopathology showed a well differentiated mucinous adenocarcinoma seen throughout the full thickness of the heavily fibrosed gall bladder wall (figure 4). Postoperative CT scan showed no evidence of tumour in the lymph nodes or the gall bladder. The patient was offered the option of surgery for gall bladder resection but declined. The patient was given post operative radiotherapy and was well months after surgery.

DISCUSSION

Most clinicians view gall bladder carcinoma as an aggressive disease with very poor prognosis.¹ Recent advances in diagnostic imaging modalities,

a better knowledge of the natural history of gall bladder disease⁹ and reports of long term survival of more than fifty percent at five years after resection surgery have influenced many authors to advocate radical surgical treatment for gall bladder malignancies. Survival depends on the tumour type and on the ability to achieve a curative resection (R0) i.e. resection with a view to a cure leaving no tumour behind locally or regionally. The overall five-year survival rate is 52% after curative resection compared to only 5% after non- curative resection. The two patients with adeno carcinoma were alive and well, but the patient with squamous carcinoma died, and the patient with carcinosarcoma has metastases. This demonstrates the more aggressive nature of the unusual tumour types. The most common clinical staging used is the TNM staging which is as follows.

T0 No evidence of primary tumour

Tis Carcinoma in situ

T1 Tumour invades lamina propria or muscle layer

T1a tumour invades lamina propria

T1b Tumour invades muscle layer

T2 Tumour invades perimuscular connective tissue limited by serosa

T3 Tumour perforates serosa or extends directly into adjacent organs i.e. liver (<2cm)

T4 Tumour extends more than 2 cm into liver and/or into two or more adjacent organs

N0 no regional lymph node metastasis

N1 Metastasis in cystic duct, pericholedochal, and/or hilar lymph nodes (i.e. in the hepatoduodenal ligament)

N2 Metastasis in peripancreatic (head only), periduodenal periportal, coeliac and/or superior mesenteric lymph nodes

M0 no distant metastasis

M1 distant metastasis

STAGE GROUPINGS

Stage0 Tis N0 M0

Stage1 T1 N0 M0

Stage2 T2 N0 M0

Stage3 T1 N1 M0, T2 N1 M0, T3 N0 M0

As laparoscopic surgery has a potential to disseminate malignancy through port sites,¹¹ it is generally advised that patients suspected preoperatively of having carcinoma should not have laparoscopic surgery but rather undergo an open exploration with potential definitive resection. However, there is a high incidence of gall bladder carcinomas which are detected for the first time at histological examination. Most of the tumours discovered after laparoscopic surgery are early T1 tumours but they may T2 tumours. The treatment for T1 disease still remains controversial^{1,4} as some of the patient with early disease (T1b) might have lymph node involvement. Thus many authors would suggest that T1a could be successfully treated by simple cholecystectomy while patients with T1b require extended cholecystectomy.⁴ For T2 disease, there is general agreement about the need for extended cholecystectomy as more than half of the patients are likely to have nodal metastases.⁵ Tumours with penetration greater than or equal to T2 discovered after laparoscopic surgery should have further imaging to rule out disseminated disease. These patients should then undergo reexploration and a radical resection for potential cure.¹² It has been shown that aggressive resection for gall bladder carcinoma discovered laparoscopically is safe and effective. The role of resectional surgery for T3 T4 lesions is controversial as there are different reports as to the survival of patients after resectional surgery. Reports are present of improved survival after radical resection for stage T4 tumours from countries like Japan¹⁰ but most reports from Europe⁵ have failed to show improved survival. Thus major resections including regional and para aortic lymphadenectomy can be recommended only for selected patients with metastases limited to regional lymph nodes.⁷ It is advisable that biopsy of para-aortic nodes is done before starting major resections as they are involved more frequently than expected and radical surgery in such patients offers no survival benefit. It is also imperative that the patients are in reasonably good health because of the high associated morbidity and mortality. Gall bladder cancers are generally not very chemo-or radio-sensitive. There have been reports suggesting that combining radiotherapy with aggressive resection for stage T4 tumours may improve survival.^{3,8} As local recurrence is the main cause of failure, preoperative chemo radiotherapy has been tried in a prospective trial with encouraging findings.¹³ Further prospective

randomised trials will be required to evaluate the role of adjuvant therapy in the form of radiotherapy or chemotherapy, and their value with different tumour types.^{5, 13}

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